IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO

THE CLEVELAND CLINIC FOUNDATION and **CLEVELAND HEARTLAB, INC.**	)	**CASE NO.: 1:15-cv-02231**
	)	
	)	**JUDGE:**
Plaintiffs,	)	
	)	
vs.	)	
	)	
TRUE HEALTH DIAGNOSTICS LLC,	)	
	)	
Defendant.		

MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

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I. INTRODUCTION

Unless enjoined by this Court, True Health's continued infringement of Cleveland Clinic and Cleveland HeartLab's patented MPO technology threatens to scuttle the new cardiovascular testing market that these patents created. Using this patented myeloperoxidase ("MPO") testing as a springboard, Cleveland HeartLab created a market segment for identifying patients at risk for heart disease through blood testing. While many lab companies partnered with Cleveland HeartLab to gain access to this market, ***True Health explicitly rejected the opportunity to acquire an existing supply agreement and instead blatantly launched an infringing test, albeit one of questionable efficacy***. Absent injunction, True Health's infringement threatens to sink not only Cleveland HeartLab's business, but the entire MPO testing market.

Taking MPO testing from invention to market has been a long, expensive and arduous process. Cleveland HeartLab has not only spent millions to educate treating physicians, it has also obtained FDA clearances, established essential lab protocols for handling MPO test specimens and developed the accepted methods for reporting and interpreting test data. It also established the quality control and patient care standards that are now customary in its MPO testing market. With heart disease being the top killer in the United States, it is hard to understate the clinical value of the patented MPO testing.

Unlike conventional tests that only look for potential causes of heart disease, MPO testing looks for an actual symptom of heart disease—blood vessel inflammation. This testing can find potentially dangerous levels of inflammation by analyzing the MPO biomarker that is found in bodily fluids, such as the blood stream. Recognizing this unique approach, the entire heart disease testing market has respected and even acquiesced to the MPO testing patents—with the exception of one new player. True Health not only ignores the MPO testing patents, it

displays studied disregard for proper lab procedures and testing protocols, apparently uses substandard materials to perform its infringing MPO tests, and carelessly reports results with ever-shifting test ranges. ***True Health's patent infringement may actually be dangerous***.

The actions of True Health are nothing more than reckless profiteering at the direct expense of patient health. Without intervention by this Court, True Health's patent infringement could cause permanent damage to the MPO testing market that Cleveland Clinic and Cleveland HeartLab laboriously created. Accordingly, this request for a TRO and preliminary injunction should be granted.

II. BACKGROUND

A. Cardiovascular Disease—America's Number One Killer

Physicians today rely more and more on lab tests to diagnose disease, guide treatment, and manage patient health risks. The role of lab testing is underscored by the fact that lab test results account for almost 70 percent of the data associated with a patient's medical record. (Declaration of Jake Orville ¶ 6, attached as Exhibit A ("Orville Decl.")) Testing of blood samples provides some of the most critical patient information, with blood sampling and analysis becoming a ubiquitous testing medium. By testing blood samples, a physician can obtain much predictive data—information that can be used to help manage a patient's well-being while also avoiding costly and unnecessary treatments and prescriptions. Moreover, wellness and disease management—the medical ecosystem associated with the vast majority of healthcare delivered in this country—is based on identifying and managing health risk. (Orville Decl. ¶ 6.) A crucial part of this risk identification and management originates from lab tests.

A particularly prevalent use of blood tests for risk identification and wellness management is testing for Cardiovascular disease (CVD). CVD is the number-one killer of both

men and women in the United States. (Orville Decl. ¶ 6.) While many different tests are used to identify and manage risks associated with CVD, the most commonly accepted lab test for identifying CVD risk is the ubiquitous cholesterol test. (Declaration of Dr. Marc Penn ¶ 15, attached as Exhibit B ("Penn Decl.")) While cholesterol testing has proven to be a solid tool for identifying potential CVD risk, it is not without its limits. Measures of cholesterol are used to define risk, and the lowering of cholesterol by diet, lifestyle and medicines has been successful in lessening the risk of heart attack. (*Id.*)

However, the pervasive lowering of cholesterol has led to an interesting point in the history of American CVD medicine: tens of millions of cholesterol tests are performed each year in the U.S., but approximately 50 percent of people who experience a heart attack or stroke previously displayed normal cholesterol levels when tested. (*Id.* ¶ 16.) Put another way, cholesterol testing by itself is not effective for properly identifying many instances of patient CVD risk. While other methods exist to identify CVD risk, they are very expensive and impractical to implement in a larger population. There has thus been a glaring need for testing that is easy to administer, like a cholesterol test, but that provides a better level of predictive data to catch missed CVD risk.

B. The Development of MPO Testing

In 2003, researchers at the top heart institute in the United States, The Cleveland Clinic Foundation ("CCF"), developed a new test to address the shortcomings of cholesterol testing. (Penn Decl. ¶ 9.) This new test provides a more refined picture of CVD risk than cholesterol alone. (*Id.* ¶ 17.) It identifies high risk for having a heart attack or stroke in patients that cholesterol-only testing often labels as having little or no risk. This is achieved by analyzing inflammation of the blood vessels. (*Id.*) Inflammation of the blood vessel wall is an early

symptom of many types of CVD that occurs before cholesterol-caused blockages. (*Id.*) At its simplest level, inflammation testing is looking for symptoms of existing disease no matter the cause, while cholesterol is merely looking at one potential cause of CVD. (*Id.*)

This innovative lab test, called Myeloperoxidase or MPO testing, measures inflammation (including its onset) in the blood vessel cell wall, and thus susceptibly of blood vessels forming dangerous blood clots and blockages that can lead to a heart attack. These findings were so profound that the study used to prove MPO testing's clinical value was published in one of the most prestigious medical journals in the world: The New England Journal of Medicine. Marie-Luise Brennan et al., *Prognostic Value of Myeloperoxidase in Patients with Chest Pain*, 349 NEW ENG. J. MED. 1595 (2003).

To maintain its ranking as the top cardiovascular healthcare center in the country, CCF has historically invested enormous amounts of resources in research. (*Id.* ¶ 22.) This research has resulted in breakthrough clinical inventions like MPO testing. Recognizing the importance of this discovery, CCF filed a series of patent applications to protect the MPO testing invention that have ultimately become issued patents. (*See id.* ¶ 4.) CCF also determined that the MPO testing inventions were worthy of commercial efforts and helped to organize a group of local and national investors as well as physicians to launch Cleveland HeartLab in 2009 as the exclusive licensee of these patents and patent applications. (*Id.* ¶ 10.) And it was launched with a sole mission: ***establish MPO testing as effective and accepted mechanism for identifying CVD risk***.

C. Cleveland HeartLab Revolutionizes Cardiovascular Disease Testing

Cleveland HeartLab's MPO testing is changing the paradigm for analyzing the risk of heart disease by ***focusing on inflammation—an actual symptom of heart disease***—instead of only measuring levels of a potential cause. However, it is necessary to educate physicians to

achieve adoption of this new test. Commencing at its formation and carrying through to the present, Cleveland HeartLab is conducting a long and exhaustive campaign to educate physicians on the benefits and innovations of MPO testing. (Penn Decl. ¶ 10.)

Achieving industry-wide adoption of a test like MPO often takes 10-12 years and can require tens of millions of dollars of investment not only in education, but also in further research and establishment of strict lab standards that ensure reliability and repeatability. (Orville Decl. ¶ 7.) In other words, industry-wide adoption of a CVD test requires consistency across the industry. This is exactly the process that Cleveland HeartLab has undertaken as it has built this new segment of the CVD testing market. Specific to these efforts, Cleveland HeartLab is conducting ongoing medical and scientific studies, has sought FDA approvals and has obtained Medicare reimbursement status for MPO testing. (*Id.* ¶ 8.) It has also developed and implemented stringent manufacturing and quality standards, conducted dedicated educational programs and assembled a well-trained sales, marketing and educational team. (Penn Decl. ¶¶ 26, 29-38, Orville Decl. ¶ 8.) None of this has come easy, and to protect the market segment that it created, Cleveland HeartLab (and CCF) has invested heavily in building and expanding the intellectual property protecting the MPO innovations. This is reflected by a robust MPO testing patent portfolio including the asserted patents.

As physicians begin to recognize the value and importance of MPO testing for identifying CVD risk, Cleveland HeartLab has experienced significant growth. When the company was founded in 2009, Cleveland HeartLab had only eight employees and shared lab space with several other startups. (Orville Decl. ¶ 9.) Today, the company leases a dedicated 30,000 square-foot state of the art facility and has 140 employees:

Cleveland HeartLab's Cleveland Facility, Lab and Staff

(*Id.* ¶¶ 9-10.)

Cleveland HeartLab's staff includes over 30 people focused on marketing, supporting and educating clinicians all over the U.S. on the value and benefits of MPO testing. (*Id.* ¶ 9.) Cleveland HeartLab's top-tier clinical education team has spent an enormous amount of time educating physicians—often one-on-one—and even offers physicians the opportunity to meet with key CVD thought leaders at its annual educational conferences. For example, through Cleveland HeartLab's "peer-to-peer" support program, PhDs at Cleveland HeartLab engage in open-ended discussions with physicians who are interested in using MPO testing in their practices. (Penn Decl. ¶ 31.) These discussions range from questions about test results for a specific patient to requests for face-to-face meetings to go over a series of test results on a

number of patients so that the physicians feel comfortable with their understanding of how to implement and utilize MPO testing. (*Id.*)

Cleveland HeartLab also continues to invest in advancing clinical evidence of MPO's role in predicting CVD risk. For example, a recent peer-reviewed published study in The Journal of Medical Economics demonstrated that MPO testing in combination with other standard tests could lead to millions of dollars in healthcare savings. *See* M. S. Penn, et al., *The Economic Impact of Implementing a Multiple Inflammatory Biomarker-Based Approach to Identify, Treat, and Reduce Cardiovascular Risk*, 18 J. MED. ECON. 483 (2015). All of these efforts have been very effective at building the company, but are also very expensive and require investment of significant time.

Commercial success of a lab test also requires that a large audience adopt the test. Getting the MPO testing story out can tax the resources of a relatively young company like Cleveland HeartLab. Therefore, Cleveland HeartLab adopted a commercialization strategy that is predicated on creating a market segment for its test by, at times, offering MPO testing to other clinical laboratories. By offering its MPO capabilities to other labs, Cleveland HeartLab hopes that market acceptance of its test will be accelerated thuse reaching more at-risk patients. Currently some labs send patients' blood samples to Cleveland HeartLab for analysis. (Orville Decl. ¶ 11.)Also, when the volume is large enough, Cleveland HeartLab manufactures a high-quality MPO testing kits for sale to other laboratories. (*Id.*) That said, all of this is performed under the strict lab standards for MPO testing mandated by Cleveland HeartLab in order to ensure consistency among labs authorized to perform MPO testing. (*Id.*)

To date, Cleveland HeartLab has invested millions of dollars to develop and manufacture its high-quality MPO test and testing kit. (*Id.* ¶ 12.) It has also obtained FDA clearance to

distribute an MPO testing kit to other labs. (*Id.*) Ongoing clinical studies to support its FDA clearance approach their fifth year—underscoring both the efforts needed to produce clinical data to support a high-quality MPO test and the company's efforts to champion MPO. (*Id.*) Additionally, Cleveland HeartLab continues to advance MPO testing with further investment over the last three years to develop a high-throughput product that will hopefully open the door to additional large-scale MPO testing. (*Id.*)

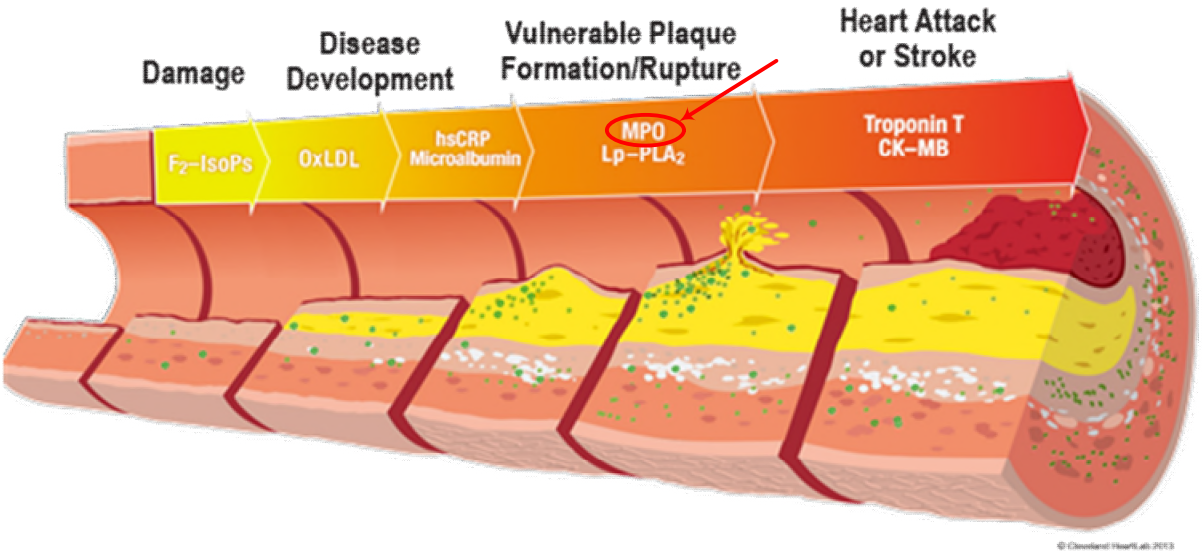
Finally, perhaps the easiest way to quantify Cleveland HeartLab's success is the number of MPO test run per year. In 2009, its first year of existence, Cleveland HeartLab performed only a few hundred MPO tests. (*Id.* ¶ 13.) Fast-forward six years and Cleveland HeartLab will perform ***hundreds of thousands*** of MPO tests in 2015. (*Id.*) This essentially exponential growth in tests has resulted Cleveland HeartLab creating an MPO segment in the CVD market that is gaining traction—but this position is now unfairly under attack by an unscrupulous patent infringer.

D. Understanding MPO and Cleveland HeartLab's Innovations

One innovative feature of the patented MPO test is that it helps identify individuals who are in need of aggressive treatment while culling potential "false positives" (i.e., those who do not require such treatment, but whose cholesterol profile might indicate to the contrary). To provide a more complete assessment of CVD, the inventors of the MPO testing patents began looking at ways to determine test levels, apply these levels to identify at-risk patients and then to correlate them into a treatment plan for at-risk CVD patients. The result: MPO could be used to more accurately identify at-risk patients and ultimately lead to formulation of a better treatment plan. (Penn Decl. ¶ 11.)

MPO is an enzyme released by white blood cells when inflammation occurs in the body. (*Id.* ¶ 18.) It serves to "amplify" the inflammatory response leading to oxidation of proteins and cholesterol. (*Id.*) When an artery wall is damaged or becomes inflamed, MPO is released into the blood stream in an effort to kill bacteria. (*Id.*) Also, MPO can be detected before any significant damage is done. The body will usually release MPO well before cholesterol leads to plaque rupture causing further plaque growth (and potential blockage) or occurrence of a traumatic event like heart attack or stroke. (*Id.*)

Cleveland HeartLab's approach is to assist the physician in recognizing whether the patient is at risk for heart disease and where the patient falls on a risk spectrum. This is illustrated below:



(Orville Decl. ¶ 14, annotation added.)

Patients can have risk limited to lifestyle, for example smoking or diet. (Penn Decl. ¶ 19.) However, these risks do not always indicate that patients have advanced disease with evidence of inflamed or vulnerable plaque. (*Id.*) This type of patient could demonstrate elevated

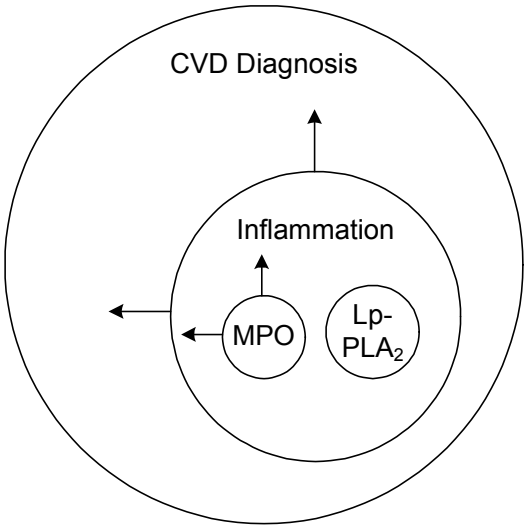
MPO levels (or in some cases elevated Lp-PLA2 levels). (*Id.*) Defining the acuity of risk and not presence of possible risk allows the treating physician to make more accurate and timely decisions regarding timing and aggressiveness of treatment. (*Id.*) It also addresses the limitations of standard cholesterol screenings by providing a more complete picture.

E. The MPO Patents

This incredibly valuable invention has been protected with numerous patents, but at least three U.S. patents are asserted here: U.S. Patent No. 7,223,552 ("the '552 Patent") (attached as Exhibit C), U.S. Patent No. 7,459,286 ("the '286 Patent") (attached as Exhibit D) and U.S. Patent No. 8,349,581 ("the '581 Patent") (attached as Exhibit E) (collectively, "the MPO Patents"). All three cover differing MPO testing inventions. The '552 Patent stems from an April 12, 2001 patent application and issued on May 29, 2007. Competitors have challenged the validity of the '552 Patent by subjecting it to two separate reexamination proceedings with the USPTO. The proceedings, however, failed and the validity of the '552 Patent was confirmed in both reexams. (*See* Ex. C, Ex Parte Reexamination Certificates.) In fact, the patent's validity has been confirmed three times—first in its initial examination and subsequently in the two reexaminations.

The '286 Patent stems from an October 22, 2003 patent application and issued on December 2, 2008. The '581 Patent is a continuation of the application that led to the '286 Patent and issued on January 8, 2013. The MPO testing Patents analyze the myeloperoxidase biomarker in order to predict potential for heart disease and determine potential treatments. Simply put, the patents aims require determining a level of MPO found in the bodily sample from a patient, comparing that MPO level with levels of MPO in control subjects to see if the patient has elevated levels of MPO that is indicative of CVD risk.

F. MPO's Effect on the CVD Market



The potential of MPO was first recognized in 2003, but it did not achieve market success until Cleveland HeartLab was formed. The current state of the CVD Diagnosis market is illustrated to the right. (Orville Decl. ¶ 15.) Cholesterol testing dominates the market and for many patients has proven to be a useful test. (Penn Decl. ¶ 15.) To provide a more refined picture of CVD risk (and identify patients missed by cholesterol screening), inflammation testing is on the rise. While inflammation holds much promise as an indicator of CVD, the methods for determining inflammation are limited to Lp-PLA2 (also known as the PLAC® test) and MPO. PLAC® testing has been on the market for many years and only measures a specific type of inflammation. (*Id.* ¶ 21.) MPO provides the "rest of the picture" and not only identifies at-risk patients missed by cholesterol, but also those missed by PLAC®. (*Id.* ¶ 22.) Thus, MPO has become a growing market segment for CVD diagnosis.

Cleveland HeartLab's efforts (and expenditures) have led to more and more physicians adopting MPO. (*Id.* ¶ 24.) As a result, the CVD market segment for inflammation testing—and MPO in particular—has been rapidly growing since 2009.

G. The CVD Market Respects the MPO Patents

As the MPO market segment continues to grow, several competitors in the laboratory testing market sector now utilize MPO testing under the auspices of Cleveland HeartLab. For instance, one of the largest laboratory services companies in the United States, Quest Diagnostics, uses Cleveland HeartLab's MPO test services under a referral testing agreement.

(Orville Decl. ¶ 16.) The Quest Agreement contains strict provisions on collection and maintenance of blood samples. (*Id.*) It also gives Cleveland HeartLab the express and unfettered right to reject specimens that were not properly collected. (*Id.*) Agreements with other lab companies have similar provisions. (*Id.*) This is done to maintain the integrity of the test. If the integrity is compromised, physicians may very well stop using MPO testing. In addition to Quest, several other lab companies either use Cleveland HeartLab as its MPO testing lab or purchase Cleveland HeartLab MPO testing kits. (*Id.* ¶ 11.)

H. Cleveland HeartLab's MPO Supply Agreement with HDL

One large lab company in particular used Cleveland HeartLab as it source for MPO testing for several years. In July of 2010, Health Diagnostics Lab ("HDL") entered into a "Laboratory Services Agreement" (attached as Exhibit F) with Cleveland HeartLab. Under this agreement, HDL engaged Cleveland HeartLab to perform all of HDL's MPO tests for physicians and clinics it serviced. (Ex. F § 1.1.) At the time of this agreement, HDL was a major lab services company. This Laboratory Services Agreement included stringent protocols for specimen collection and gave Cleveland HeartLab the right to reject improperly collected or prepared specimens. (*Id.* § 1.2.) This Laboratory Services Agreement also clearly spelled out the existence of the MPO testing patent portfolio, including the patents at issue. (*Id.* § 7.) Additionally, HDL not only acknowledged these patent rights, but also agreed not to infringe or dispute these patents. (*Id.*)

This relationship lasted for five years and resulted in important revenue for Cleveland HeartLab. (Orville Decl. ¶ 18.) It also expanded the use of MPO testing and grew the MPO testing market segment. Unfortunately, towards the end of 2014, HDL's marketing practices were investigated by the Department of Justice. (*Id.*) As a result of this investigation, a large

DOJ settlement was entered against HDL and its outside sales team. (*Id.*) Ultimately, this fine and other changes to its business forced HDL to bankruptcy proceedings in June of 2015. *See In re Health Diagnostic Lab, Inc.*, No. 15-32919-KRH (Bankr. E.D. Va. June 7, 2015). Shortly thereafter, HDL decided to cease being a going concern and put its assets up for sale.

I. True Health Diagnostics Purchases HDL's Assets—Except for the MPO Supply Agreement

True Health Diagnostics was formed around March 2014. It is a lab services company that according to its website performs the cardiovascular lab testing market as well testing for genetic disorders, diabetes and metabolic conditions. (True Health Website, attached as Exhibit G.) It apparently offers a large menu of tests and until very recently, did not offer MPO testing. (In fact, its entrance into the MPO market is so recent that MPO testing is not listed as an available test on its website.) (Orville Decl. ¶ 19.)

True Health's CEO contacted Cleveland HeartLab's CEO Jake Orville in the summer of 2014 regarding the potential purchase of MPO testing kits. (Id. ¶ 20.) During discussions in May and June of 2014, True Health acknowledged that Cleveland HeartLab is the source of the patented MPO testing and that, as a CVD lab, True Health desired access to these tests. (*Id.*) True Health's CEO even visited Cleveland HeartLab's Cleveland facility to discuss the potential purchase of MPO test kits. (*Id.*) These talks, however, were unavailing. (*Id.*)

During the HDL bankruptcy proceedings, however, True Health bid on and ultimately purchased certain HDL assets as part of a "stalking bidder process." Under this process, True Health submitted a bid listing exactly which HDL assets it was bidding on and which ones it was excluding. While True Health's bid included HDL's customer list (which included HDL's MPO testing customers), ***True Health expressly excluded Cleveland HeartLab's MPO Supply***

Agreement with HDL. *See* Notice, *In re Health Diagnostic Lab, Inc.*, No. 15-32919-KRH , at 5 (Bankr. E.D. Va. September 30, 2015), ECF No. 545 (attached as Exhibit H) (highlight added). The bid also included an asset purchase agreement that specifically stated True Health is not a successor to HDL. Order Approving APA, *In re Health Diagnostic Lab, Inc.*, No. 15-32919-KRH , at 13 (Bankr. E.D. Va. September 17, 2015), ECF No. 512.

The bankruptcy court approved True Health's bid of $37 million on September 10, 2015, with the assets to transfer on September 30, 2015. *See* Notice of Successful Bid, *In re Health Diagnostic Lab, Inc.*, No. 15-32919-KRH , at 1 (Bankr. E.D. Va. September 17, 2015), ECF No. 489. Thus, when the asset purchase agreement went into effect on the last day of September, the Laboratory Services Agreement was not purchased. Accordingly, True Health is unquestionably not covered by this agreement or operating under any authority from Cleveland HeartLab to use the inventions of the MPO Patents. Despite rejecting the agreement's safe-harbor (that could have been purchased in the auction), True Health launched an infringing MPO test after getting its hands on HDL's MPO customer list.

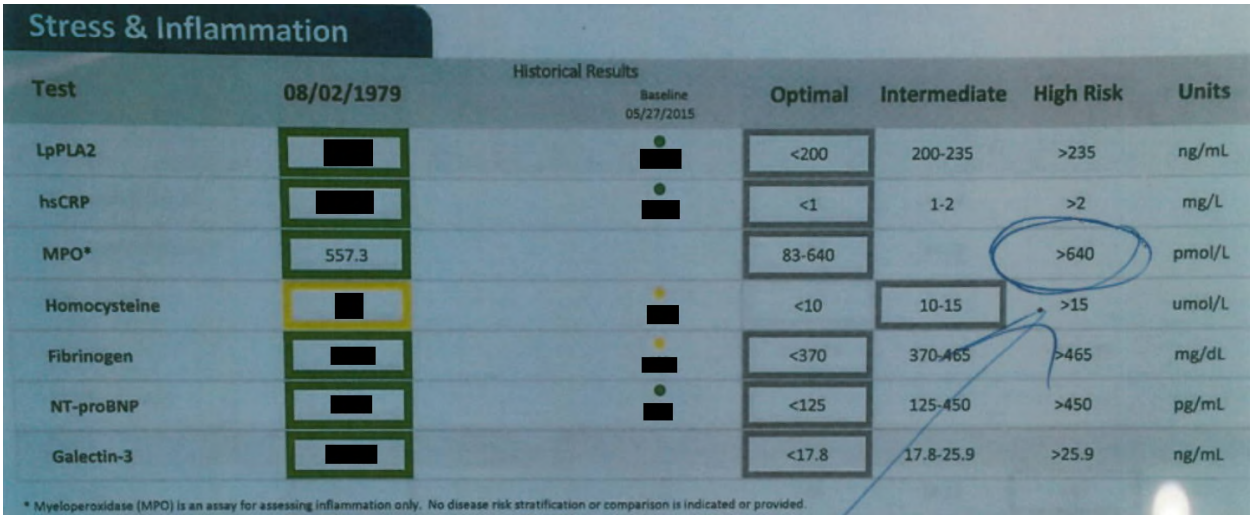
Given that the MPO patents are the foundation of Cleveland HeartLab's efforts to build the inflammation market segment, a company that violates the MPO patents runs the risk of destroying the market. Moreover, by rejecting the HDL Laboratory Services Agreement, ***True Health knows that is it not authorized to run the patented MPO test***. An unauthorized lab gives rise to questions about testing procedure and quality control. To hopefully head off these issues, Cleveland HeartLab's CEO, Jake Orville, wrote to True Health's CEO regarding concerns that True Health would be offering an unlicensed MPO test. To date, True Health has never responded to this September 14, 2015 email (attached as Exhibit I).

J. True Health's Recent Introduction of Unauthorized MPO Testing

In view of True Health's silence to the Cleveland HeartLab's September 14, 2015 email and its rejection of the HDL Laboratory Services Agreement, Cleveland HeartLab became increasingly concerned that True Health was conducting MPO testing. In October, Cleveland HeartLab anecdotally learned that at least one True Health sales person was representing to former HDL customers that True Health was offering an MPO test ***from Cleveland HeartLab and was Cleveland HeartLab's exclusive partner***. (Orville Decl. ¶ 22.) This led to an investigation by Cleveland HeartLab to determine if True Health was actually offering MPO testing.

In mid-October, Cleveland HeartLab acquired a lab test showing that True Health was in fact conducting MPO tests. (Orville Decl. ¶ 23.) This was followed by several more lab reports—all of them having differing formats, and two including the HDL logo while listing a True Health employee as the lab director responsible for the test. (Orville Decl. ¶¶ 24-26.) Patent infringement by itself is sufficient grounds for complaint, but Cleveland HeartLab's concerns run much deeper. It is troubling that the reports all use different ranges for establishing the risk of a CVD event. This indicates a lack of quality. In other words, the ever-changing ranges showing that True Health is not providing clinical value and is not properly performing MPO testing to ascertain CVD risk assessment. (*See* Penn Decl. ¶ 43.) Also, this is an indication that True Health is not adhering to standard laboratory regulations and procedures. By running a test with no quality standards and shifting clinical reference ranges, True Health is not just putting the entire MPO market segment at risk. True Health is putting patient care at risk.

The earliest known True Health MPO lab report is dated (printed) "10/5/2015" (attached as Exhibit J). It lists the MPO range as "high risk" at over 640 pmol/L:



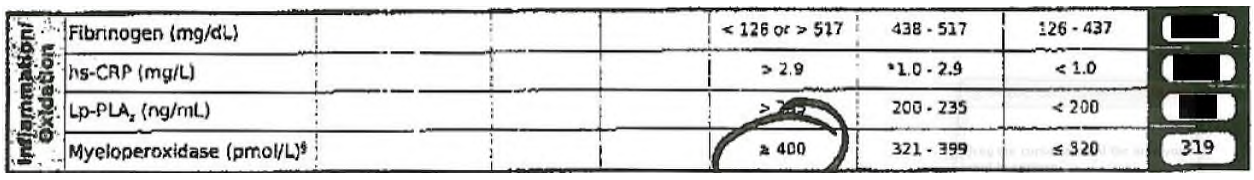
Stress & Inflammation

Test	Historical Results 08/02/1979	Historical Results Baseline 05/27/2015	Optimal	Intermediate	High Risk	Units
LpPLA2	[redacted]	[redacted]	<200	200-235	>235	ng/mL
hsCRP	[redacted]	[redacted]	<1	1-2	>2	mg/L
MPO*	557.3		83-640		>640	pmol/L
Homocysteine	[redacted]	[redacted]	<10	10-15	>15	umol/L
Fibrinogen	[redacted]	[redacted]	<370	370-465	>465	mg/dL
NT-proBNP	[redacted]	[redacted]	<125	125-450	>450	pg/mL
Galectin-3	[redacted]		<17.8	17.8-25.9	>25.9	ng/mL

* Myeloperoxidase (MPO) is an assay for assessing inflammation only. No disease risk stratification or comparison is indicated or provided.

Suspiciously, the lab report lists that for the MPO test, the test is only for "assessing inflammation" and "[n]o disease risk is indicated or provided." This only appears for the MPO test despite other inflammation tests such as LpPLA2 also appearing on the report. Although True Health is trying to steer away from the MPO testing patents, later-discovered lab reports omit this disclaimer. Of course, True Health's dubious "disclaimer" assumes that the treating physician reading this report will ignore that True Health is a CVD lab company offering tests for the CVD market. Given that True Health has knowledge of the patents (evidenced by its initial desire to partner with Cleveland HeartLab and its subsequent rejection of the HDL Laboratory Services Agreement) and its doctors use this test to treat heart disease, it stands that True Health knows this is a violation of the MPO patents.

Three more True Health MPO lab reports have recently been uncovered. Two of them are on HDL letterhead, but dated after the asset purchase, and listing True Health's lab director as the lab director for the test (attached as Exhibits K and L, respectively):



Inflammation/ Oxidation	Fibrinogen (mg/dL)				< 126 or > 517	438 - 517	126 - 437	[redacted]
	hs-CRP (mg/L)				> 2.9	*1.0 - 2.9	< 1.0	[redacted]
	Lp-PLA$_2$ (ng/mL)				> [redacted]	200 - 235	< 200	[redacted]
	Myeloperoxidase (pmol/L)§				≥ 400	321 - 399	≤ 320	319

Inflammation/ Oxidation	Fibrinogen (mg/dL)		[redacted]		< 126 or > 517	438 - 517	126 - 437
	hs-CRP (mg/L)	[redacted]			> 2.9	1.0 - 2.9	< 1.0
	Lp-PLA$_2$ (ng/mL)		[redacted]		[redacted]	200 - 235	< 200
	Myeloperoxidase (pmol/L)[5]	448			≥ 332	256 - 331	≤ 255

In all likelihood, these are True Health run tests invoiced to customers that came from the HDL customer list that was purchased in the asset auction. The fourth report is on True Health letterhead (attached as Exhibit M):

Others	Result	Flag	Reference Interval
Myeloperoxidase (pmol/L)[5]	181		< 557

All of these MPO tests were performed within the last few weeks. Again, particularly troubling to Cleveland HeartLab, each lab report lists a different MPO range. In other words, there is no consistency between the True Health MPO tests.

Based on the differing MPO ranges, it appears that True Health is not performing consistent tests or reporting consistent results. It also appears that True Health is not properly treating samples nor following the correct lab procedures. This approach is at least lackadaisical and perhaps even reckless as it could result in false positives and potentially false negatives. Confusion caused by these differing and inconsistent ranges will lead to physicians discontinuing use of the test. (Penn Decl. ¶ 43. *See also* Declaration of Dr. Mark. C. Houston ¶ 23, attached as Exhibit N ("Houston Decl.")) Also, the varied ranges calls into question True Health's quality control practices and adherence to standard lab procedures and practices.

Moreover, there is an unspoken and fundamental agreement between the laboratory industry and the ordering physician: the same tube of blood should yield the same result, and the

result should be accompanied with accurate clinical information, ***independent*** of the performing laboratory. It has also been well documented in medical literature that patient blood samples must be drawn in a specific blood-collection tube. (Penn Decl. ¶ 26.) Using an incorrect collection tube can cause a false-positive test result. (Penn Decl. ¶ 27.) This would lead the physician to order unnecessary and expensive testing or potentially harmful treatments based on a test result caused by incorrect blood-collection procedures.

Cleveland HeartLab has discovered that True Health uses a blood-collection tube intended for molecular genetic testing instead of the recommended tube. This could lead to mishandling of the MPO test. It also is running tests that are not authorized by nor subject to Cleveland HeartLab's quality control standards, as evidenced by the differing MPO ranges shown on the reports.

Given that Cleveland HeartLab has maintained stringent control protocol—which have been accepted by the industry as evidenced by the HDL and Quest agreements—it is of great concern that True Health is running shoddy tests. This is causing a large negative effect on MPO testing, the research of CCF and Cleveland HeartLab and finally, most importantly patient care. And because most of the MPO market views Cleveland HeartLab as the sole source of MPO as well as the MPO innovator, any misstep by True Health will in all likelihood be blamed on Cleveland HeartLab—especially in view of True Health's insinuation that it is a partner of Cleveland HeartLab. Additionally, True Health's infringement may mushroom and entice other labs to become "fast followers" and likewise infringe the MPO testing patents as well. Moreover, such a misstep could denigrate MPO as a whole and render all of Cleveland HeartLab's work to create the market moot.

III. JURISDICTION AND VENUE

To Cleveland HeartLab's knowledge, at least eight clinics in Northeast Ohio are currently purchasing lab services from True Health. (Orville Decl. ¶ 27.) At least one physician has stated that he is specifically purchasing MPO tests from True Health. (*Id.*) Further, True Health maintains a sales agent in Ohio who apparently has sold and is offering to sell testing services, including MPO testing to physicians and clinics in Ohio. (*Id.* ¶ 28.)

A. Law on Jurisdiction and Venue for Patent Infringement Actions

Personal jurisdiction in patent infringement cases is governed by Federal Circuit law rather than regional circuit law. *3D Sys. v. Aarotech Labs., Inc.*, 160 F.3d 1373, 1377 (Fed. Cir. 1998). The Federal Circuit applies a two-prong test to determine whether the exercise of personal jurisdiction over an out-of-court state defendant is proper: 1) the defendant must be amenable to process in the forum state and 2) the exercise of personal jurisdiction must comport with federal due process. *LSI Industries, Inc. v. Hubbell Lighting, Inc.*, 232 F. 3d 1369, 1371 (Fed. Cir. 2000).

1. Amenability to Process in Ohio (The Ohio Long-Arm Statute)

Ohio's long-arm statute provides several specific bases for the exercise of personal jurisdiction over a non-resident defendant. *See* Ohio Rev. Code § 2307.382. These bases for jurisdiction include "[t]ransacting any business in this state," § 2307.382(A)(1), "[c]ontracting to supply services or goods in this state," § 2307.382(A)(2), or "[c]ausing tortious injury by an act or omission in this state," § 2307.382(A)(3).

This District has construed "[t]ransacting any business" to broadly include where the transaction relates to the cause of action. *See Puronics, Inc. v. Clean Res. Inc.*, 2013 U.S. Dist. LEXIS 5414, at *5 (N.D. Ohio Jan. 14, 2013) (finding jurisdiction based on defendant's

shipment of five orders of products over six years to Ohio and defendant's multiple purchase orders from Ohio-based entities). The District has also used a two-factor analysis to determine whether an out-of-state defendant has "transacted business" under Ohio's long-arm statute, considering 1) whether the defendant initiated the transaction and 2) whether the parties conducted negotiations in the forum state or the transaction's terms affect the forum state. *Hitachi Med. Sys. Am., Inc. v. St. Louis Gynecology & Oncology, LLC*, NO. 5:09-CV-2613, 2011 U.S. Dist. LEXIS 17022, at *12 (N.D. Ohio Feb. 22, 2011).

Jurisdiction is also proper based on "tortious injury" within the state. Patent infringement is a tort created by federal statute, and the injury from the tort occurs where the product is sold or offered to be sold. *Beverly HillsFan Co. v. Royal Sovereign Corp.*, 21 F.3d 1558, 1571 (Fed. Cir, 1994). This District has held that Ohio's long-arm statute is satisfied when both the tortious act and the injury occur in Ohio. *Canplas Indus., Ltd. v. InterVac Design Corp.*, No. 1:13 CV 1565, 2013 U.S. Dist. LEXIS 166277, at *4 (N.D. Ohio Nov. 22, 2013) (citing *Gor-Vue Corp. v. Hornell Elektrooptik AB*, 634 F. Supp. 535, 537 (N.D. Ohio 1986)).

2. Due Process

Due process requires that the defendant "have certain minimum contacts with [the forum state] such that the maintenance of the suit does not offend traditional notions of fair play and substantial justice." *Int'l Shoe Co. v. Washington*, 326 U.S. 310, 316 (1945) (internal quotation marks omitted). In patent cases, this standard is satisfied where the defendant purposefully directed its activities at residents of the forum, (2) the claim arises out of or relates to those activities, and (3) assertion of personal jurisdiction is reasonable and fair. *3D Sys.*, 160 F.3d at 1378.

Moreover, a party cannot escape jurisdiction by using an independent sales agent in the forum state. The Supreme Court has stated that "marketing [a] product through a distributor who has agreed to serve as the sales agent in the forum State" is sufficient to show "intent or purpose to serve the market in the forum State." *Asahi Metal Indus. Co. v. Superior Court*, 480 U.S. 102, 112 (1987). Accordingly, this District has found purposeful availment where the defendant purposefully sold its products in Ohio. *See Puronics*, 2013 U.S. LEXIS 5441, at *20. Furthermore, even if no actual sales are made, an offer to sell an infringing product constitutes patent infringement, and thus an offer to sell in the forum state can establish specific jurisdiction. *3D Sys.*, 160 F.3d at 1379.

Finally, with regard to reasonableness, Ohio has a significant interest in discouraging patent infringement within its boundaries, "and also has a substantial interest in cooperating with other states to provide a forum for efficiently litigating [this] cause of action." *Step2 Co. v. Parallax Grp. Int'l*, No. 5:08CV2580, 2010 U.S. Dist. LEXIS 97659, at *7 (N.D. Ohio Sept. 17, 2010).

B. This Court Has Jurisdiction Based on True Health's Infringing Sales in Ohio

True Health's current sales of MPO testing in Ohio satisfy the state's long-arm jurisdiction statue. These transaction were initiated by True Health and the negotiations were in Ohio. The transactions also gave rise to the cause of action, as they include sales of infringing MPO tests. Further, jurisdiction is proper because an infringing sale (i.e., the "tortious injury") occurred in Ohio. Also, True Health is maintaining an Ohio sales agent—evidence of intent or purpose to sell MPO testing in this state.

Second, True Health's sales of MPO testing in Ohio satisfies the federal Due Process standard. True health purposely directed its activities at Ohio by engaging a sales agent here and

selling infringing MPO tests (the basis for the present claim) to Ohio customers. Jurisdiction is fair because Ohio has an interest protecting patent rights within its borders.

C. Venue is Proper Because this Court Has Personal Jurisdiction

Finally, venue is proper where "the defendant resides, or where the defendant has committed acts of infringement and has a regular and established place of business." 28 U.S.C. § 1400(b). A corporate defendant is deemed to reside in any judicial district where it is subject to personal jurisdiction. 28 U.S.C. § 1391(c). Thus, "[v]enue in a patent action against a corporate defendant exists wherever there is personal jurisdiction." *Trintec Indus. v. Pedre Promotional Prods.*, 395 F.3d 1275, 1280 (Fed. Cir. 2005). Without issue, venue in the Northern District of Ohio is proper.

IV. ARGUMENT

A. Legal Standards for Injunction and TRO

The "right to maintain exclusivity" is "a hallmark and crucial guarantee of patent rights deriving from the Constitution itself." *Apple Inc. v. Samsung Elecs. Co.*, No. 2014-1802, 2015 U.S. App. LEXIS 16536, *14 (Fed. Cir. Sept. 17, 2015). Injunctive relief provides a mechanism for "taking advantage of these fundamental rights." *Id.* at *15 (citing *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 393 (2006)).

Temporary restraining orders are appropriate to preserve the status quo pending a hearing on preliminary injunction. *First Tech. Safety Sys. v. Depinet*, 11 F.3d 641, 650 (6th Cir. 1993). Likewise, a preliminary injunction serves to "preserve the relative positions of the parties until a trial on the merits can be held." *Univ. of Tex. v. Camenisch*, 451 U.S. 390, 395 (1981). A plaintiff seeking preliminary injunction must prove: 1) reasonable likelihood of success on the

merits; 2) irreparable harm; 3) a balance of equities in its favor; and 4) the public interest favors injunction. *Winter v. NRDC, Inc.*, 555 U.S. 7, 20 (2008). Courts, exercising sound discretion, "must balance the competing claims of injury and must consider the effect on each party of the granting or withholding of the requested relief." *Id.* (internal quotation removed). The same factors are analyzed in considering a TRO. *See AIG Aviation v. Boorom Aircraft*, 142 F.3d 431 (6th Cir. 1998).

B. Likelihood of Success on the Merits

A likelihood of success on the merits for patent infringement suits requires a two-prong analysis covering both infringement and validity. *Oakley, Inc. v. Sunglass Hut Int'l*, 316 F.3d 1331 (Fed. Cir. 2003). The court must construe and compare the claims to the alleged infringing activity. *Id.* at 1339. The court must also compare the claims to the alleged prior art for validity.

1. Infringement

"[A] grant of preliminary injunction does ***not* require proof of infringement beyond all question**." *Ill. Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679, 682 (Fed. Cir. 1990) (emphasis added). Instead, the patentee need only show that success in establishing infringement is "more likely than not." *Trebro Mfg. v. FireFly Equip.*, LLC, 748 F.3d 1159, 1166 (Fed. Cir. 2014). As stated above, the terms of the claims must first be construed. If each and every step of the claim is present either literally or by equivalents, then there is infringement.

Here the claim construction is straightforward—most of the terms should simply be afforded their "plain and ordinary" meaning. The only terms requiring construction at this preliminary stage are "MPO activity" and "MPO mass." Applying these construed claims to True Health's own lab reports show that True Health is indeed infringing the MPO Patents.

While True Health is infringing numerous claims of the MPO Patents, for the convenience of the Court, Cleveland HeartLab is limiting its injunction request to five claims:

- Claims 11 and 15 of the '552 Patent;
- Claims 21 and 22 of the '286 Patent; and
- Claim 5 of the '581 Patent.

This limited approach stands to reason. These claims are relatively straightforward, require limited claim construction and all elements are met by True Health's own lab reports. Moreover, these claims belong to patent families that have been vetted numerous times against a host of prior art—severely limiting any validity challenge. Thus, Cleveland HeartLab can show it is reasonably likely to prevail at trial on its infringement charge against True Health.

i. Claim Construction of the terms "MPO Activity" and "MPO Mass"

Except for "MPO Activity" and "MPO Mass", all of the claim terms should simply be afforded their plain and ordinary meaning. Based on the MPO testing Patents' specifications, "MPO activity" means that a substrate is provided to assess the enzymatic activity of the MPO. (Houston Decl. at 9). Likewise, "MPO mass" means the amount of MPO molecules in a sample, measured, for example, in picomoles per liter (pmol/L). A "molecule count" type assay, such as an ELISA (enzyme-linked immunosorbent assay) can be used to determine MPO mass. (Houston Decl at 10.)

ii. True Health Infringes Claims 11 and 15 of the '552 Patent

Claims 11 and 15 cover methods for assessing a test subject's risk for having CVD. Claim 11 reads as follows:

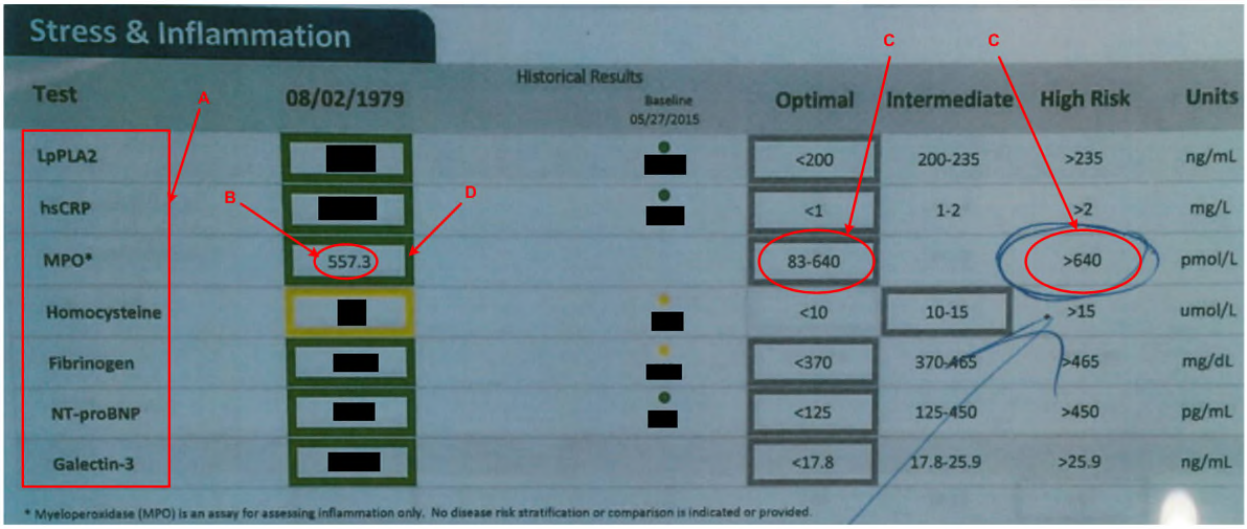
> 11. A method of assessing a test subject's risk of having atherosclerotic cardiovascular disease comprising:

> comparing levels of myeloperoxidase in a bodily sample from the test subject with levels of myeloperoxidase in comparable bodily samples from control subjects diagnosed as not having the disease, said bodily sample being blood, serum, plasma, blood leukocytes selected from the group consisting of neutrophils, monocytes, sub-populations of neutrophils, sub-populations of monocytes, or any combination thereof;
>
> wherein elevated levels of myeloperoxidase in the bodily sample from the test subject relative to the levels of myeloperoxidase in comparable bodily samples from control subjects is indicative of the extent of the test subject's risk of having atherosclerotic cardiovascular disease.

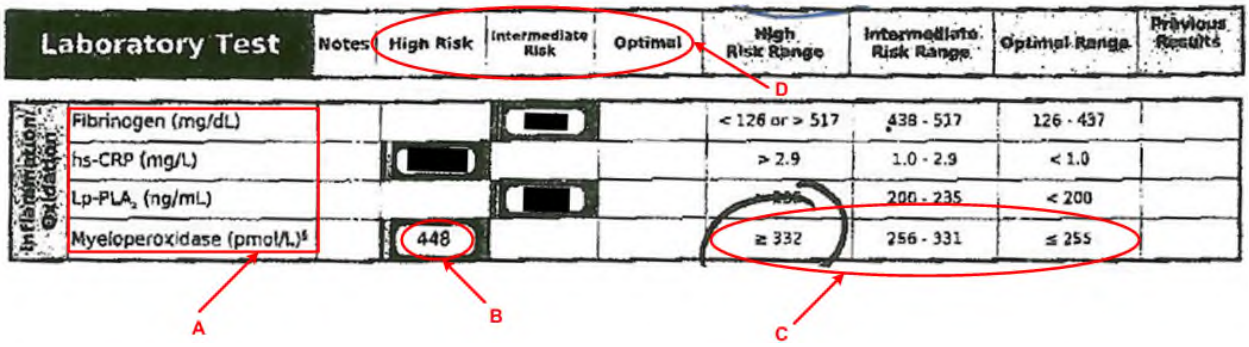
The claims thus require implicitly determining a level of MPO found in the bodily sample of a test subject, comparing that MPO level with levels of MPO in a control subject where elevated levels of MPO is indicative of a test subject's risk of having CVD. Additionally, the test sample can be whole blood or a number of blood derivatives including serum, plasma, differing types of white blood cells or any combination of these.

The True Health Lab Reports show that it is practicing these steps and thus infringing. All four reports show that a bodily sample is acquired, an MPO level is determined, that MPO level is compared to a reference range. In three of these reports, the ranges are listed as "optimal", "intermediate" and "high" risk although the actual ranges vary. They also state that the level is measured in pmol/L. The final report lists "result", "flag" and "reference interval." No matter the semantics used, these reports satisfy the elements of claim 11.

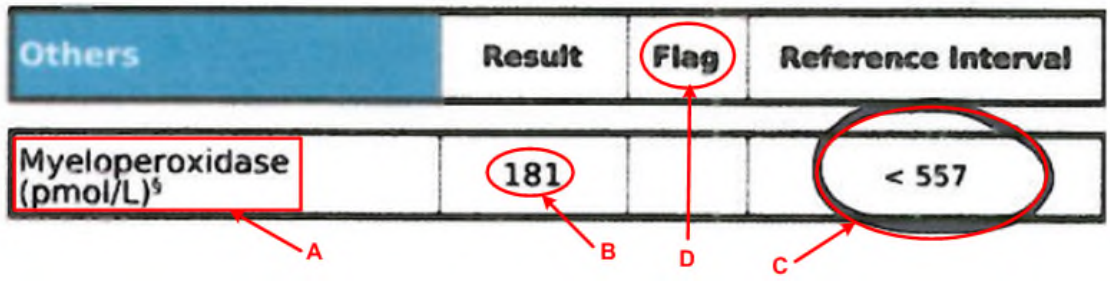
These reports directly assess the test subject's risk of CVD. For convenience of the Court, the reports are shown below annotated with letters representing elements of the asserted claims. The reports evidence that an MPO level (A) has been determined from a bodily sample (B), that a control group is used via reference ranges (C) and that elevated levels of MPO from the bodily sample comparable to the control group is indicative of CVD risk by altering the color surrounding the MPO result, placing the MPO result in a specific risk column or placing an indicator in a flag column (D):



Ex. J (annotations added)



Ex. L (annotations added)



Ex. M (annotations added)

For example, as seen in the reports, if the test is above a certain number (640 pmol/L in Report 1, 332 pmol/L in Report 2 or 557 pmol/L in Report 3) then the treating physician knows that the patient is at risk. Further, based on the other tests shown in these reports, there is little

question that the tests were performed on a blood sample. (Houston Decl. ¶ 13. *See also* True Health Website, attached as Exhibit O ("if you do extreme exercise the day before your blood test"); True Health Website, attached as Exhibit P ("The nurse or phlebotomist will draw your blood.")) In other words, each and every limitation of Claim 11 is met on the face of these reports.

As seen below, a similar infringement analysis holds for Claim 15. (Claim 15 depends from Claim 14, so it includes all of the limitations of this claim, as shown below.)

Claim 15 (depends from claim 14)	**True Health's Lab Reports**
14. A method of assessing a test subject's risk of developing a complication of atherosclerotic cardiovascular disease comprising:	Each Report includes an indicator for CVD risk (D).
determining levels of myeloperoxidase (MPO) activity, myeloperoxidase (MPO) mass, or both in a bodily sample of the test subject, said bodily sample being blood, serum, plasma, blood leukocytes selected from the group consisting of neutrophils and monocytes, or any combination thereof;	The Reports include a test for MPO (A) and a result (i.e., determination of) MPO levels (B). The result is measured as an MPO mass (pmol/L). MPO tests are almost always taken from blood samples (Houston Decl. ¶ 13), and True Health heavily advertises its blood-testing services. (Exs. O, P.)
wherein elevated levels of MPO activity or MPO mass or both in the test subject's bodily sample as compared to levels of MPO activity, MPO mass, or both, respectively in comparable bodily samples obtained from control subjects diagnosed as not having the disease indicates that the test subject is at risk of developing a complication of atherosclerotic cardiovascular disease.	The Reports include risk ranges (C) based on comparable bodily samples from a control group. (Houston Decl. ¶ 14) The risk ranges are a measure of MPO mass (pmol/L). A comparison of the test result (B) to the risk range (C) is denoted by an indicator (D) that indicates CVD risk.

15. The method of claim **14**, wherein the test subject's risk of developing a complication of atherosclerotic cardiovascular disease is determined by comparing levels of myleperoxidase mass in the test subject's bodily sample to levels of myeloperoxidase mass in comparable samples obtained from the control subjects.	The result (B) and risk range (C) are measured as an MPO mass (pmol/L). MPO tests are almost always taken from blood samples (Houston Decl. ¶ 13), and True Health heavily advertises its blood-testing services. (Exs. O, P.) Also, Ex. L specifically states that it is ***not*** a urine sample.

Accordingly, each and every limitation of claims 1 and 15 of the '552 Patent is evidenced in the lab reports. THD is infringing these claims.

iii. True Health Infringes Claims 21 and 22 of the '286 Patent

Claims 21 and 22 of the '286 Patent likewise cover methods for assessing a test subject's risk for having CVD. The charts below shows where each limitation of the claims is evidenced in the above-pictured lab reports:

Claim 21	**True Health's Lab Reports**
21. A method of assessing the risk of requiring medical intervention in a patient who is presenting with chest pain, comprising	Each Report includes an indicator for CVD risk (D).
characterizing the levels of myeloperoxidase activity, myeloperoxidase mass, or both, respectively in the bodily sample from the human patient, wherein said bodily sample is blood or a blood derivative,	The Reports include a test for MPO (A) and a result (i.e., characterization of) MPO levels (B). The result is measured as an MPO mass (pmol/L). MPO tests are almost always taken from blood samples (Houston Decl. ¶ 13), and True Health heavily advertises its blood-testing services. (Exs. O, P.)
wherein a patient whose levels of myeloperoxidase activity, mycloperoxidase mass, or both is characterized as being elevated in comparison to levels of myeloperoxidase activity, myeloperoxidase mass or both in a comparable bodily samples obtained from individuals in a control population is at risk of requiring medical intervention to prevent the occurrence of an adverse cardiac event within the next six months.	The Reports include risk ranges (C) based on comparable bodily samples from a control group. (Houston Decl. ¶ 14) The risk ranges are a measure of MPO mass (pmol/L). A comparison of the test result (B) to the risk range (C) is denoted by an indicator (D) that indicates CVD risk. A physician would understand this risk to be of a CVD event in

	the next six months. (Houston Decl. ¶ 15.)

Claim 22	**True Health's Lab Reports**
22. A method of determining whether a patient who presents with chest pain is at risk of requiring medical intervention to prevent an adverse cardiac event within the next six months comprising:	Each Report includes an indicator for CVD risk (D). A physician would understand this risk to be of a CVD event in the next six months. (Houston Decl. ¶ 15.)
comparing the level of a risk predictor in a bodily sample from the subject with a value that is based on the level of said risk predictor in comparable samples from a control population, wherein said risk predictor is myeloperoxidase activity, myeloperoxidase mass, a myeloperoxidase-generated oxidation product, or any combination thereof, and wherein said bodily sample is blood, serum, plasma, or urine,	The risk indicator (D) is based on a comparison between a result (B) that shows the level of a risk predictor in a sample and risk-range (C) that denotes comparable samples from a control group. (Houston decl. ¶ 14) The risk predictor is listed in the reports as MPO (A). MPO tests are almost always taken from blood samples (Houston Decl. ¶ 13), and True Health heavily advertises its blood-testing services. (Exs. O, P.)
wherein a subject whose bodily sample contains elevated levels of said risk predictor as compared to the control value is at risk of requiring medical intervention to prevent an adverse cardiac event within 6 months of presenting with chest pain, and	Each Report includes an indicator for CVD risk (D). A physician would understand this risk to be of a CVD event in the next six months. (Houston Decl. ¶ 15.)
wherein the difference between the level of the risk predictor in the patient's bodily sample and the level of the risk predictor in a comparable bodily sample from the control population establishes the extent of the risk to the subject of requiring medical intervention to prevent an adverse cardiac event within the next six months.	A physician would understand the level of risk of a CVD event in the next six months to correlate to the difference between the test result (B) and the risk range (C). (Houston Decl. ¶ 15.)

As shown in the above charts, the lab reports reveal that True Health is practicing each limitation of claims 21 and 22 of the '286 Patent and is thus directly infringing the claims.

iv. True Health Infringes Claim 5 of the '581 Patent

Claim 5 of the '581 Patent similarly covers methods for assessing a test subject's risk for having CVD. The chart below shows where each limitation of the claim is evidenced in the above-pictured lab reports.

Claim 5	**True Health's Lab Reports**
5. A method of determining whether a patient who presents with chest pain is at risk of requiring medical intervention to prevent an adverse cardiac event within the next six months comprising:	Each Report includes an indicator for CVD risk (D). A physician would understand this risk to be of a CVD event in the next six months. (Houston Decl. ¶ 15.)
determining the level of risk predictor in a bodily sample from the subject, wherein said risk predictor is myeloperoxidase activity, myeloperoxidase mass, a myeloperoxidase (MPO)-generated oxidation product or any combination thereof,	The Reports include a test (A) for risk predictor MPO and lists a result (i.e., level) (B). The result is an MPO mass (pmol/L).
wherein said bodily sample is blood, serum, plasma or urine,	MPO tests are almost always taken from blood samples (Houston Decl. ¶ 13), and True Health heavily advertises its blood-testing services. (Exs. O, P.)
wherein said myeloperoxidase-generated oxidation product is nitrotyrosine or a myeloperoxidase-generated lipid peroxidation product selected from hydroxy-eicosatetraenoic acids (HETEs); hydroxy-octadecadienoic acids (HODEs), F2Isoprostanes; the glutaric and nonanedioic monoesters of 2-lysoPC (G-PC and ND-PC, respectively); the 9-hydroxy-10-dodecenedioic acid and 5-hydroxy-8-oxo-6-octenedioic acid esters of 2-lysoPC (HDdiA-PC and HOdiA-PC, respectively); the 9-hydroxy-12-oxo-10-dodecenoic acid and 5-hydroxy-8-oxo-6-octenoic acid esters of 2-lysoPC (HODA-PC and HOOA-PC, respectively); the 9-keto-12-oxo-10-dodecenoic acid and 5-keto-8-oxo-6-octenoic acid esters of 2-lysoPC (KODA-PC and KOOA-PC, respectively); the 9-keto-10-dodecendioic acid and 5-keto-6-octendioic acid esters of 2-lysoPC (KDdiA-PC and KOdiA-PC, respectively); and the 5-oxovaleric acid and 9-oxononanoic acid esters of 2-lysoPC (OV-PC and ON-PC, respectively), or any combination thereof, and	Because the result (B) is an MPO mass and not and MPO-generated oxidation product, this limitation is not applicable.
comparing the level of said risk predictor in the bodily sample of the patient to the level of said risk predictor in comparable samples obtained from a control population,	A comparison of the test result (B) to a risk range (C) is denoted by an indicator (D) that indicates CVD risk. The risk-range (C) denotes comparable samples from a control group. (Houston decl. ¶ 14.)

wherein a subject whose bodily sample contains elevated levels of said risk predictor as compared to the control value is at risk of requiring medical intervention to prevent an adverse cardiac event within 6 months of presenting with chest pain.	A physician would understand the level of risk of a CVD event in the next six months to correlate to the difference between the test result (B) and the risk range (C). (Houston Decl. ¶ 15.)

The lab reports, on their face, demonstrate that True Health's MPO tests meet each limitation of Claim 5 of the '581 Patent. True Health is thus directly infringing the '581 Patent.

2. Validity

Patents are presumed valid, however, when moving for preliminary injunction, the patent owner bears the burden of "clear[ly] showing" that its patent is valid. *Nutrition 21 v. United States*, 930 F.2d 867, 870 (Fed. Cir. 1991). According to the Federal Circuit this means that the district court "must weigh the evidence both for and against validity that is available at this preliminary stage in the proceedings." *Warner Chilcott Labs. Ireland Ltd. v. Mylan Pharms., Inc.*, 451 Fed. Appx. 935, 939 (Fed. Cir. 2011) (quotation omitted). Put another way, the patentee must show that in light of the presumption of validity that inheres at trial, the patent can withstand challenges to validity at the TRO/preliminary injunction phase. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350-51 (Fed. Cir. 2001). District courts must keep in mind that a patent is presumed valid at every stage of the litigation and if the challenger fails to identify any persuasive evidence of invalidity, the very existence of the patent satisfies this prong. Here, the facts support the presumption—the MPO Patents are in all likelihood valid.

The MPO Patents have undergone exhaustive examination by the USPTO. During the examination (and reexaminations) of the MPO patents, the USPTO has reviewed literally volumes of prior art, found the patents allowable over this prior art and issued the patents. The

'552 Patent went through this examination process not just once, but three separate times. Additionally, the industry (except for True Health) has respected these patents.

It is well-established that for a TRO/preliminary injunction, industry acceptance or acquiescence of the patents, as we have here, is strong evidence of validity. *Amazon.com*, 239 F.3d at 1359. Some courts have even found that acquiescence where a patent provided "tremendous financial success" in a shorter period of time demanded issuance of a preliminary injunction. *See Zenith Labs., Inc. v. Eli Lilly & Co.*, 460 F. Supp. 812, 822 (D.N.J. 1978).

In *Zenith*, the court issued a preliminary injunction on a drug-related patent noting several factors probative of acquiescence, including recognition of validity by two licensees, availability in foreign markets, and, "most significant, four major drug companies . . . have sophisticated knowledge of [the drug] and patents, present capacity to make [the drug] and resources to litigate validity, yet they have respected the '656 Patent and refrained from infringement." *Id.* Again, this is the present case. Several companies, including one of the largest lab companies in the world, Quest Diagnostics, have acquiesced to the MPO Patents by either entering into supply agreements with Cleveland HeartLab or purchasing the patented MPO kit from the lab. This is clear acceptance/acquiescence and thus strong evidence of validity.

Also, prior adjudication upholding the validity of the patent, such as a reexamination, may provide "considerable weight" in showing validity. That said, more weight is generally given when the third-party requester was the current defendant, and when the same prior art was at issue. *Compare Auto. Prods. v. Federal-Mogul Corp.*, 11 U.S.P.Q. 2d (BNA) 1471, 1473 (E.D. Mich. 1989) *with GenDerm Corp. v. Ferndale Labs. Inc.*, 32 U.S.P.Q. 2d (BNA) 1567, 1571-72 (E.D. Mich. 1994). Here, the '552 Patent was reexamined twice. Again, this is strong evidence that in all likelihood the patent is valid.

Finally, True Health may try to justify its infringement by claiming that the MPO testing patents are invalid for including unpatentable subject matter. This challenge fails. Based on recent Supreme Court mandates, courts must "distinguish between patents that claim the 'buildin[g] block[s]' of human ingenuity and those that integrate the building blocks into something more, thereby 'transform[ing]' them into a patent-eligible invention[.]" *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014) (citation omitted) (quoting *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 132 S. Ct. 1289, 1294 (2012)). Here, the MPO patents are more than mere claiming of human building blocks—and the USPTO even issued the '581 Patent after the Supreme Court issued its new directive.

Section 101 of the Patent Act requires that patents be awarded to "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." 35 U.S.C. § 101. In applying §101, the Court should distinguish between merely "the building blocks of human ingenuity" and the patents before us here that "***integrate the building blocks into something more***[.]" *Alice*, 134 S. Ct. at 2354 (quotation omitted) (emphasis added). Following on the heels of *Mayo*, in *Alice*, the Supreme Court formulated a two-part test for distinguishing between patents that fail to meet § 101 and those that claim patent-eligible subject matter. *Id.* at 2355.

In the first step, the court determines whether the claims at issue are directed to a patent-ineligible concept such as a law of nature. *Id*. If the answer to this question is "yes", the Court should then determine whether the patent contains an "inventive concept" that can be described as an "element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Id.* (quoting *Mayo*, 132 S. Ct. at 1294). In other words, if a claim includes method steps that were (either

individually or taken together) not well-understood, not routine, and not conventional (or perhaps were new and nonobvious), then that would be a significant factor weighing in favor of eligibility.

In *Mayo*, the Supreme Court found the claims under review unpatentable because they were directed to a natural law where the steps of the claims, taken individually and together, were well-known and thus not sufficient to transform the natural law into a patentable application of that law. 132 S. Ct. at 1298. The MPO testing Patents, however, are far from this. Instead, the asserted claims of the MPO testing Patents have the inventive concept of applying a phenomenon in a combination of steps that no one had done before along with a level of specificity for performing these steps.

Here, the measuring of MPO levels to determine the risk of having atherosclerotic cardiovascular disease is not known in the prior art, the determining step is not well-understood, not routine, and not conventional, it is an "inventive concept" that makes the claims eligible for patentability. This sharply contrasts to the *Mayo* claim because the steps in the *Mayo* claim (both individually and together) were known and used in the prior art; that is, administration of that drug for that condition was known and the measurement of the metabolites resulting from administration of that drug was also known.

The determining step of the asserted claims is also very specific—unlike the *Mayo* claim. The determining steps require measurement of a closed set of specific bodily samples while in *Mayo*, the reviewed claim did not provide any specific method to determine the metabolite, nor did it specify which bodily fluid/tissue should be sampled to measure the metabolite. Thus, the MPO Patents clearly are applying a phenomenon in a combination of steps that has never been done. Also, during reexamination of the '552 Patent, evidence was submitted that MPO mass

and MPO activity as used in the claims are determined in a novel manner. (*See* Supplemental Response, Reexamination Control No. 90/009,744, at 11 (USPTO Feb. 15, 2011), attached as Exhibit Q.) The USPTO agreed with this assessment and issued the patent—exactly the type of evidence that carries the day under the second prong of *Alice*.

Accordingly, any arguments that True Health may try to raise about patentability fall far short of the mark. The claims are patentable and Cleveland HeartLab has shown that its patents are valid.

C. Irreparable Harm

A plaintiff seeking injunction must also prove that it will suffer irreparable injury during the litigation absent injunction. *Winter,* 555 U.S. at 20. The plaintiff must further show a "causal nexus" between the alleged harm and alleged infringement. *Apple Inc. v. Samsung Elecs. Co.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012). Irreparable harm may be presumed when the plaintiff clearly establishes validly and infringement. *Smith Int'l, Inc. v. Hughes Tool Corp.*, 718 F.2d 1573, 1581 (Fed. Cir. 1983).

The Federal Circuit has held that loss of goodwill (i.e., reputational damage) can constitute irreparable harm. *Douglas Dynamics, LLC v. Buyers Products Co.*, 717 F.3d 1336, 1344 (Fed. Cir. 2013). The court in *Douglas Dynamics* found that the plaintiff's "reputation as an innovator will certainly be damaged if customers found the same 'innovations' appearing in competitors' [products], particularly products considered less prestigious and innovative." *Id.* at 1344-45. The court further found that the plaintiff's reputation would be damaged if others believed it did not enforce its intellectual property rights "so that it could maintain market exclusivity." *Id.* at 1345. In sum, "[w]here two companies are in competition against one another, the patentee suffers the harm—***often irreparable***—of being forced to compete against

products that incorporate and infringe its own patented inventions." *Id.* at 1345 (emphasis added).

Monetary harm may be irreparable when it is incalculable, for example where sales of the patented product create an "ecosystem" that drives recommendations and downstream sales of other products. *Apple*, 2015 U.S. App. LEXIS 16536 at *27. Recently, the Federal Circuit overturned a denial of injunction, holding that the district court's "dismissal of evidence showing likely loss of market share and loss of access to customers was an error of law." *Trebro Mfg.*, 748 F.3d at 1170. Specifically, the Federal Circuit relied on the small market size, which constituted only three players—the patent owner, a single licensee and the infringer. *Id.* Accordingly, "every sale to [the alleged infringer] is essentially a lost sale to [the patent owner]." *Id.* Based on these facts, the Federal Circuit found that one sale, and six pre-sales constituted "a real non-speculative harm," and the loss of significant market share constituted irreparable harm. *Id.* (citing several recent Federal Circuit cases). The court rejected the defendant's argument that an ability to estimate monetary damages precluded injunction, instead finding that a loss of market share may be irrecoverable, and that continued infringement would force the patent owner to lay off employees. *Id.* at 1170-71. This is the type of irreparable damage Cleveland HeartLab faces especially because the market for MPO testing is still nascent and growing. If infringement is allowed, Cleveland HeartLab may not be able to keep financing its efforts to the grow the market—which could lead to a cascade of catastrophic events including potential layoffs.

Courts have considered several additional factors in finding irreparable harm in patent cases, including the effect of denying injunction on the patent owner's market share and whether others will be encouraged to infringe. *Certain Pressure Transmitters*, Inv. No. 337-TA-304,

USITC Pub. 2392 at 8 (Mar. 19, 1990) (Preliminary), *aff'd Rosemount, Inc. v. ITC*, 910 F.2d 819 (Fed. Cir. 1990).

Applying the present facts to this long body of case law yields one, inescapable conclusion: True Health's recent, unauthorized entry into the MPO market is irreparably harming Cleveland HeartLab. If True Health is allowed to proceed with selling their sub-standard and inconsistent test, Cleveland HeartLab faces the very real specter of injury to both the reputation of MPO as a viable test and injury to its own reputation in the market. MPO is still in its infancy as a test for CVD. While Cleveland HeartLab has quickly grown the use of the test, there are still many physicians who may be unaware of the benefits of MPO testing. A single false result in one of the True Health dubious tests could tar the entire MPO market segment. Once such a failure occurs, no amount of physician education can put the "genie back in the bottle."

Additionally, because Cleveland HeartLab is known as ***the MPO company***, any mistake in testing that True Health commits will likely (and unfairly) implicate Cleveland HeartLab. This is exactly the type of damage to reputation and goodwill that the Federal Circuit found to be irreparable harm in *Douglas Dynamics*. That court also noted that the patent holder suffers irreparable harm when the market believes that it will not enforce its patents. Moreover, when two companies compete, the patentee can suffer harm if it is forced to compete against its own, patented products. All of these instances are present here. If True Health is allowed to infringe with impunity, other MPO users such as Quest Diagnostics may follow True Health's lead and stop using Cleveland HeartLab as its source for patented MPO. Also, Cleveland HeartLab is the innovator—not True Health. That position as the leader in the market is invaluable and it risks destruction if True Health is not enjoined.

Thus, True Health is exacerbating the problem by usurping market share derived solely from its infringement. Brazenly, True Health acquired this "instant" market share by ***purchasing HDL's customer list in the exact same transaction where it rejected HDL's MPO Supply Agreement with Cleveland HeartLab***. In one fell swoop, True Health gained access to HDL's customers without being required to use Cleveland HeartLab for the patented MPO—a direct causal nexus exists between True Health's decision to infringe the patents and Cleveland HeartLab's loss of market. And in doing this, True Health is encouraging others to follow fast and likewise infringe the MPO Patents. Why not? It is a quick way to avoid costs while taking market share. This loss of market share by itself warrants a finding of irreparable harm. When viewed in connection with the damage to reputation and having to compete against its own invention, a clear case of irreparable harms has been made—a clear case warranting injunction.

D. Balance of Hardships

Generally, if a court has found a likelihood of success on the merits and irreparable harm, the court will grant injunction unless the balance of hardships tips decidedly in favor of the defendant. *See Ill. Tool*, 906 F.2d at 683. Seeing that True Health knew it would be infringing the MPO patents, it is hard-pressed to now claim that it will suffer some unwarranted hardship. To the contrary, it is Cleveland HeartLab that will suffer hardship—including potentially grave consequences to the company—absent an injunction stopping True Health's entrance into the MPO market via a calculated decision to infringe the MPO Patents.

For example, the Federal Circuit rejected a defendant's alleged hardships where "the harms were almost entirely preventable and were the result of [the defendant's] calculated risk to launch its product pre-judgment." *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006) (quotation omitted). Particularly, in *Sanofi-Synthelabo*, the defendant "engage[d] in

an at-risk launch" of a product knowing infringement would occur before the merits of the litigation would be addressed. *Id. See also Apple*, 2015 U.S. App. LEXIS 16536 at *27 ("[F]orcing [the patentee] to compete against its own patented invention . . . 'places a substantial hardship' on a patentee, especially here where it is undisputed that it is essentially a two-horse race.") (quoting *Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1156 (Fed. Cir. 2011)). To contrast, the balance of hardships has been found to favor the accused infringer where the patent owner was a large corporation but the accused infringer was a "fledgling company" that would be put out of business if an injunction issued. *Bell & Howell Document Mgmt. Prods. Co. v. Altek Sys.*, 132 F.3d 701, 704 (Fed. Cir. 1997). *See also Intel Corp. v. ULSI Sys. Tech.*, 995 F.2d 1566, 1568 (Fed. Cir. 1993). That is certainly not the case here.

Any hardships alleged by True Health were entirely preventable and without issue the product of its calculated decision to reject the HDL Laboratory Services Agreement. It has only been offering this test for mere weeks. Moreover, True Health offers many other tests in addition to its recent foray into MPO testing. It has many other ways of generating revenue that do not involve infringing the MPO testing Patents. In marked contrast to True Health, Cleveland HeartLab is suffering immediate and irreparable hardship. It is losing market share, suffering damage to its reputation and is essentially forced to compete against its own patented inventions. Without issue, the balance of hardship tips decidedly in Cleveland HeartLab's favor—further warranting issue of immediate relief.

E. Public Interest

The final prong for consideration is where the public interest lies. Here, the public interest lies in top-quality medical innovations that are administered correctly and subject to accepted lab standards. Copycat products, dubious quality and questionable lab protocols cannot

be said to be in the public interest. "[T]he public interest ***nearly always*** weighs in favor of protecting property rights in the absence of countervailing factors, especially when the patentee practices his inventions." *Apple*, 2015 U.S. App. LEXIS 16536 at *30 (emphasis added).

Specifically, for the healthcare industry, the public interest is ***not*** served when competitors piggyback, at little or no cost, off innovative patentees that "devote large sums to invention and product improvement." *Eli Lilly & Co. v. Premo Pharm. Labs.*, 630 F.2d 120, 138 (3d Cir. 1980). While, in some cases, courts have found that the public interest favors availability of alternative, competing medical devices, *see, e.g.*, *Datascope Corp. v. Kontron Inc.*, 786 F.2d 398, 401 (Fed. Cir. 1986), more often courts find that the public interest favors medical research and development supported by patent property rights. *See, e.g.*, *ADA Health Found. v. Bisco, Inc.*, 24 U.S.P.Q. 2d (BNA) 1524, 1531 (N.D. Ill. 1992) (finding that grant of an injunction would "prevent [the plaintiff] from scaling back on its research efforts" and that the plaintiff's existing licensees "can adequately satisfy the market's demand for such a product").

Even if it were in the public interest for True Health customers to have access to MPO testing, it is True Health's conscious decision to infringe, not this Motion, that may deny MPO testing to its customers. True Health had the clear opportunity to purchase the existing Cleveland HeartLab supply agreement along with other purchased assets, but True Health deliberately chose not to do so. Cleveland HeartLab can adequately supply the MPO market. This is especially true given that it ***was*** the ultimate supplier for the customer base that True Health gained access to through the HDL auction—where it also rejected the safe harbor of the Supply Agreement and instead chose infringement. The public interest should not favor such a deliberate attack on patent rights. To hold otherwise would be to provide cart blanche for

pharmaceutical and medical-device companies to infringe patents in the name of "public interest."

V. CONCLUSION

Cleveland Clinic and Cleveland HeartLab have made a strong showing that all four TRO/preliminary injunction factors weigh decidedly in their favor. Thus, a TRO/preliminary injunction should issue. Finally, given that the potential harm True Health might incur is minimal, The plaintiffs also requests that any necessary bond be similarly small.For the above reasons, CCF and Cleveland HeartLab request a TRO/Preliminary.

Injunction.

Dated: November 12, 2015

Respectfully submitted,

/s/ Todd R. Tucker

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CERTIFICATE OF SERVICE

I hereby certify that on November 12, 2015, a copy of the foregoing document was electronically filed. Notice of this filing will be sent to counsel of record for all parties by operation of the Court's Electronic Filing System. Parties and their counsel may access this filing through the Court's Electronic Filing System. Additionally, a copy is being hand-served on Defendant by a process server on November 13, 2015.

/s/ Todd R. Tucker

One of the Attorneys for Plaintiff